PTO-1390 (Rev. 07-2005) Approved for use through 03/31/2007. OMB 0651-0021 U. S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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#### ATTORNEY'S DOCKET NUMBER TRANSMITTAL LETTER TO THE UNITED STATES 65645(46590) DESIGNATED/ELECTED OFFICE (DO/EO/US) U.S. APPLICATION NO. (if known, see 37 CFR 1.5) CONCERNING A SUBMISSION UNDER 35 U.S.C. 371 INTERNATIONAL APPLICATION NO. INTERNATIONAL FILING DATE DATE CLAIMED PCT/JP2004/017995 26 November 2004 27 November 2003 TITLE OF INVENTION METHOD OF ESTIMATING TOXICITY OF DRUG APPLICANT(S) FOR DO/EO/US Kenji Takami et al. Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information: 1. X This is a FIRST submission of items concerning a submission under 35 U.S.C. 371. This is a SECOND or SUBSEQUENT submission of items concerning a submission under 35 U.S.C. 371. 2. This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below. The US has been elected (Article 31). A copy of the International Application as filed (35 U.S.C. 371 (c)(2)) 5. X is attached hereto (required only if not communicated by the International Bureau). has been communicated by the International Bureau. X is not required, as the application was filed in the United States Receiving Office (RO/US). An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)). 6. X is attached hereto. a. x has been previously submitted under 35 U.S.C. 154(d)(4). Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) are attached hereto (required only if not communicated by the International Bureau). a. b. have been communicated by the International Bureau. have not been made; however, the time limit for making such amendments has NOT expired. C. have not been made and will not be made. d. An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). 9 10. An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). Items 11 to 20 below concern document(s) or information included: An Information Disclosure Statement under 37 CFR 1.97 and 1.98. 12. An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. A preliminary amendment. An Application Data Sheet under 37 CFR 1.76. 14. x 15. A substitute specification. A power of attorney and/or change of address letter. A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821 – 1.825. 17. × A second copy of the published International Application under 35 U.S.C. 154(d)(4). 18 A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4). 19

## IAP20 Rec'd PCT/PTO 26 MAY 2006

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U.S. APPLICATION NO A RESTAURANT OF 15 8			INTERNATIONAL APPLICATION NO. PCT/JP2004/017995			ATTORNEY'S DOCKET NUMBER 65645(46590)				
20. x Other items or information:  Figures 1 - 7 (7 sheets); Sequence Listing (44 pages); Sequence Diskette; Sequence Statement (2 pages); English Translation of PCT Request (5 pages); Copy of Cover Page of Published PCT Application No. WO 2005/052154 A1; Copy of International Search Report (Form PCT/ISA/210) (3 pages); Copy of Form PCT/IB/301, PCT/IB/304, & PCT/IB/308; Return Receipt Postcard.										
The following fees have been submitted								CALCULATIONS PTO USEONLY		
21. x Basic national fee (37 CFR 1.492(a))								00.00		
22. X Examination fee (37 CFR 1.492(c))  If the written opinion prepared by ISA/US or the international preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4)\$0  All other situations \$200								\$ 200.00		
23. x Search fee (37 CFR 1.492(b))  If the written opinion of the ISA/US or the international preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4) \$0  Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority \$100  International Search Report prepared by an ISA other than the US and provided to the Office or previously communicated to the US by the IB. \$400  All other situations \$500							\$ 400.00			
	TOTAL OF 21,						\$ 9	00.00	0	
Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing in compliance with 37 CFR 1.821(c) or (e) or computer program listing in an electronic medium) (37 CFR 1.492(j)).  The fee is \$250 for each additional 50 sheets of paper or fraction thereof.										
Total Sheets	Extra Sheets	nets Number of each additional 50 or fraction thereof (round up to a whole number)				RATE				
61 - 100 = /50 =			x \$250,00			\$				
Surcharge of \$130 for furnishing any of the search fee, examination fee, or the oath or declaration after the date of commencement of the national stage (37 CFR 1.492(h)).							\$			
CLAIMS NUMBER FILED NUMBER EXTRA RATE					RATE					
Total claims 13 - 20 =		13 - 20 =		×			0.00			
Independent claims 5 - 3 =		5 - 3 =		2 x 200.00			400.00			
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			)	+ 360.00			360.00			
TOTAL OF ABOVE CALCULATIONS =							\$ 1,660.00			
Applicant claims small entity status. See 37 CFR 1.27. Fees above are reduced by ½.										
SUBTOTAL =							\$ 1,6	60.00	P [	
Processing fee of \$130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(i)).								\$		
TOTAL NATIONAL FEE							\$ 1,660.00			
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property										
\$										
TOTAL FEES ENCLOSED =							\$ 1,660.00			
							Amount to refunded:	be	\$	
						Amount to be charged \$				
							,			

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a. A check in the amount of \$ to cover	THE 20 THE GPUI/PIO 26 MAY 2006 the above fees is enclosed.
	in the amount of \$1,660.00 to cover the above fees.
	onal fees which may be required, or credit any overpayment to Deposit this sheet is enclosed.
d. Fees are to be charged to a credit card. WARNING: Inform should not be included on this form. Provide credit card	nation on this form may become public. Credit card information information and authorization og PTO-2038
filed an granted to restore the International Application to pendi	not been met, a petition to revive (37 OFR 1.137(a) or (b)) must be ing status.
SEND ALL CORRESPONDENCE TO:	SIGNATURE
David G. Conlin EDWARDS ANGELL PALMER & DODGE LLP P.O. Box 55874	, than M. Sanda Bh S
Boston, Massachusetts 02205 (617) 439-4444	Jorlathan M. Sparks, Ph.D.  NAME
CUSTOMER NUMBER: 21874	53,624 REGISTRATION NUMBER
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PTO/SB/17 (01-06)

Approved for use through 7/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no person are required to respond to a collection of information unless it displays a valid OMB control number. Completè if Known Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818). Not Yet Assigned Application Number FEE TRANSMITTAL Concurrently Herewith Filing Date For FY 2006 Kenji Takami First Named Inventor Examiner Name Not Yet Assigned Applicant claims small entity status. See 37 CFR 1.27 N/A Art Unit 65645(46590) **TOTAL AMOUNT OF PAYMENT** 1,660.00 Attorney Docket No. METHOD OF PAYMENT (check all that apply) Money Order None Other (please identify): Check Credit Card Edwards Angell Palmer & Dodge LLP Deposit Account Number: 04-1105 Deposit Account Name: х For the above-identified deposit account, the Director is hereby authorized to: (check all that apply) Charge fee(s) indicated below Charge fee(s) indicated below, except for the filing fee Charge any additional fee(s) or underpayment of x Credit any overpayments fee(s) under 37 CFR 1.16 and 1.17 FEE CALCULATION (All the fees below are due upon filing or may be subject to a surcharge.) 1. BASIC FILING, SEARCH, AND EXAMINATION FEES **EXAMINATION FEES FILING FEES SEARCH FEES Small Entity Small Entity Small Entity** Fees Paid (\$) **Application Type** Fee (\$) Fee (\$) Fee (\$) Fee (\$) Fee (\$) Fee (\$) 200 100 Utility 300 150 500 250 100 50 65 Design 200 100 130 200 100 300 150 160 80 Plant 300 500 250 600 300 Reissue 150 100 Provisional 200 0 0 2. EXCESS CLAIM FEES Small Entity Fee (\$) Fee (\$) Fee Description Each claim over 20 (including Reissues) 50 25 Each independent claim over 3 (including Reissues) 200 100 Multiple dependent claims 360 180 **Multiple Dependent Claims Total Claims** Extra Claims Fee (\$) Fee Paid (\$) Fee Paid (\$) 13 Fee (\$) - 20 = HP = highest numer of total claims paid for, if greater than 20. 360.00 360.00 Fee Paid (\$) Extra Claims Fee (\$) 400.00 2 × 200.00 HP = highest numer of independent claims paid for, if greater than 3. 3. APPLICATION SIZE FEE If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s). Fee Paid (\$) **Total Sheets** Extra Sheets Number of each additional 50 or fraction thereof Fee (\$) 61 \_\_\_ - 100 = \_\_ \_\_ (round up to a whole number) x /50 4. OTHER FEE(S) Fees Paid (\$) Non-English Specification, \$130 fee (no small entity discount) Other (e.g., late filing surcharge): 1631 Basic National Stage fee
1633 National Stage Examination Fee - all other ... 300.00 200.00 642 National Stage Search Fee - search report ... 400.00 SUBMITTED BY Registration No. 53,624 (617) 439-4444 Telephone Signature (Attorney/Agent) Name (Print/T han 🕅 Strarks, Ph.D. Date May 26, 2006

**40/**581008

### AP20 Rec'dPCT/PTO 26 MAY 2006

Application No. (if known): Not Yet Assigned

Attorney Docket No.: 65645(46590)

#### Certificate of Express Mailing Under 37 CFR 1.10

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mail, Airbill No. EV 755 070 597 US in an envelope addressed to:

MS PCT Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

On May 26, 2006
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Typed or printed name of person signing Certificate

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Transmittal Letter to the United States Designated-Elected Office (3 pages)

Fee Transmittal (1 page) Application Data Sheet (

Specification excluding claims (50 pages), Claims (3 pages), Abstract (1 page)

Figures 1 - 7 (7 sheets) Sequence Listing (44 pages)

Sequence Diskette

Sequence Statement (2 pages)

English Translation of PCT Request (5 pages)

Copy of Cover Page of Published PCT Application No. WO 2005/052154 A1 (1 page)

Copy of International Search Report (Form PCT/ISA/210) (3 pages) Copy of Form PCT/IB/301, PCT/IB/304, & PCT/IB/308 (5 pages total)

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